Remarks

Applicants have amended Claim 9 and its dependent Claims 10-18 to depend on Claim 1. This amendment adds no new matter.

The Office Action sets forth a requirement for restriction under 35 U.S.C. §§ 121 and 372 between:

Group I, Claims 1-8, drawn to a composition comprising activated protein C and a chelating agent;

Group II, Claims 9-18, drawn to a composition comprising activated protein C, a diluent, and a chelating agent;

Group III, Claim 20, drawn to a process for making a lyophilized, drawn to a process for making a lyophilized composition comprising activated protein C and a chelating agent;

Group IV, Claim 21, drawn to a process for making a lyophilized composition comprising activated protein C, a bulking agent, and a chelating agent;

Group V, Claim 22, drawn to a process of using a lyophilized composition comprising activated protein C comprising adding a diluent comprising a chelating agent;

Group VI, Claim 23, drawn to a process of using a lyophilized composition comprising activated protein C and a bulking agent comprising adding a diluent comprising a chelating agent;

Group VII, Claim 24, drawn to a method of treating a patient in need thereof; and

Group VIII, Claim 25, drawn to a use of a composition comprising treating thrombotic disorders.

Applicants elect, with traverse, to prosecute Group I, Claims 1-9. Applicants further note that Claim 25, and therefore Group VIII, was canceled in the preliminary amendment filed on September 1, 2004.

Applicants traverse the requirement for restriction on the grounds that the inventions listed in Groups I-VII do relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, unity of invention is fulfilled by the inventions sharing a corresponding technical feature. The inventions share the technical feature of a pharmaceutical composition or formulation comprising activated protein C and a chelating agent. In particular, the inventions share the special technical feature of including a chelating agent in a pharmaceutical composition comprising activated protein C. Through this inclusion of a chelating agent, each of claimed inventions, considered as a whole, have a feature that defines a contribution made over the prior art.

Contrary to the assertion put forth in the Office Action, the compositions of Groups I-VI are not known in the art. The referenced teaching of Foster et al., US Patent 5,516,650 (Foster *et al.*), admittedly teaches compositions comprising activated protein C and EDTA. However, Foster *et al.*, unlike the present invention, does not teach a pharmaceutical composition comprising activated protein C and EDTA. Rather, Foster *et al.* teaches a composition resulting from purification of activated protein C prior to formulation of activated protein C in a pharmaceutical composition. This aspect is evident from the disclosure of Foster *et al.* at column 4, lines 1-5:

> The proteins described within the present invention may be used as active therapeutic substances, including use in the regulation of blood coagulation. Further, these protein (*sic*) may be combined with a physiologically acceptable carrier and/or diluent to provide suitable pharmaceutical compositions. (emphasis added)

Furthermore, this point is reiterated by Foster *et al.* at column 9, line 62, to column 10, line 5, which includes the statement "The protein C or activated protein C of the present invention may be used in pharmaceutical compositions for topical or intravenous application." (emphasis added) Thus, the pharmaceutical compositions of the present invention were not disclosed or suggested by Foster *et al.*

The Office Action further asserts that lyophilized compositions of activated protein C were known in the prior art, as evidenced by the disclosure of Bartl et al., US Patent 5,001,069 (Bartl et al.). Applicants acknowledge that Bartl et al. provides an example of lyophilized compositions of activated protein C. However, Bartl et al. does not teach or suggest pharmaceutical compositions of lyophilized activated protein C, nor does Bartl et al. teach a lyophilized composition containing activated protein C and a chelating agent. Rather, Bartl et al. at column 6, lines 11-14 teaches a lyophilized composition of activated protein C from purified protein C fractions eluted from a sizing column in 1% acetic acid. Bartl et al., as stated in column 1, lines 8-10 "is concerned with a process for the photometric determination of protein C and/or protein S activity, especially in plasma." Thus, Bartl et al. is concerned with examining protein C from plasma, and does not teach or suggest a pharmaceutical composition of protein C, let alone one which contains activated protein C and a chelating agent.

In view of the above, Applicants respectfully submit that the compositions of Groups I-VI were not known in the art. The inventions in the present application therefore contain the special technical feature of a pharmaceutical composition or formulation comprising activated protein C

and a chelating agent. As such, Applicants' inventions relate to a single inventive concept under PCT Rule 13.1.

The Office Action asserts that Groups I and II are drawn to two distinct compositions. In response, Applicants have amended Claim 9 and its dependent Claims 10-18 to depend on Claim 1, obviating the distinction between Groups I and II. As described in PCT Rule 13.4, it is permitted to include a reasonable number of dependent claims, claiming specific forms of the invention claimed in an independent claim, even where the features of any dependent claim could be considered as constituting in themselves an invention. As permitted by Rule 13.4, Group II now reasonably depends on Group I, thereby rendering a new, single Group I.

The Office Action sets forth that Groups III and IV are drawn to methods of production that do not necessarily result in the compositions of Groups I and II, which are not required to be lyophilized. Applicants respectfully assert that unity of invention requires a technical relationship involving one or more of the same or corresponding technical features. Groups III and IV share with Groups I and II the technical feature of a pharmaceutical composition or formulation containing activated protein C and a chelating agent. Thus, unity of invention is fulfilled among Groups I-IV.

Groups V and VI are asserted in the Office Action to be drawn to methods of use that do not necessarily require the compositions of Groups I and II or those made by the methods of Groups III and IV. However, as explained above, unity of invention is fulfilled when inventions share one or more special technical feature(s). The inventions of Groups V and VI share with Groups I-IV the technical feature of a pharmaceutical composition or formulation containing activated protein C and a chelating agent. Thus, unity of invention exists between Groups V and VI and Groups I-IV.

Group VII is asserted in the present action to lack unity of invention with Groups I-VI on the basis that the compositions of Groups I-VI are known in the art. As detailed above, the compositions of Groups I-VI are not known in the art. Thus, unity of invention exists between Group VII and Groups I-VI.

In view of the above, Applicants respectfully submit that Groups I-VII related to a single general inventive concept under PCT Rule 13.1, as they contain the same special technical feature under PCT Rule 13.2. Accordingly, Applicants request withdrawal of the restriction requirement under 35 U.S.C. §§ 121 and 372.

The Office Action further set forth a requirement to elect a single disclosed species for prosecution on the merits with respect to a bulking agent, a buffer, and a salt. Claims 1-24 are

held to be generic, as the species are asserted to not be art-recognized equivalents pursuant to PCT Rule 13.2, as described in PCT Administrative Instructions, Annex B, Part 1(f)(i)(B)(2). Applicants respectfully submit that the Markush grouping in Claims 4, 15, 5, 16, 8, and 19 fulfills the requirements of PCT Rule 13.2. As described in PCT Administrative Instructions, Annex B, Part 1(f)(iii), all alternatives belong to a recognized class of compounds when there is an expectation that members of the class will behave in the same way in the context of the claimed invention. In the present invention, each of the group of listed bulking agents in Claims 4 and 15 would be recognized by one of skill in the art to similarly behave as a bulking agent in the context of the claimed invention. Likewise, the groups of buffers in Claims 5 and 15 and salts in Claims 8 and 19 respectively would be recognized to behave similarly in the context of the claimed invention and achieve the same intended result. Thus, the species listed in the claims do relate to a single general inventive concept under PCT Rule 13.1.

While disagreeing with the requirement of species election, to expedite prosecution Applicants provisionally elect sucrose as a bulking agent, sodium citrate as a buffer, and sodium chloride as a salt as the species for prosecution on the merits. Based on the action's characterization of claims 1-24 being generic, Applicants list Claims 3, 4, 14, and 15 as readable on the elected species of bulking agent, Claims 5, 6, 16, and 17 as readable on the elected species of buffer, and Claims 7, 8, 18, and 19 as readable on the elected species of salt.

The Office Action has also acknowledged that in accordance with 37 CFR § 1.141, upon allowance of a generic claim, Applicants are entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of the allowed generic claim.

Conclusion

Having addressed all outstanding issues, Applicants respectfully request entry and consideration of the foregoing amendments which place the application in condition for allowance. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is invited to telephone the undersigned at the number below.

Respectfully submitted,

Thomas LaGrandeur
Attorney for Applicants
Registration No. 51,026
Phone: 317-651-1527

Eli Lilly and Company
Patent Division
P.O. Box 6288
Indianapolis, Indiana 46206-6288

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